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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,627	09/14/2001	Luigi Naldini	131.14-US-WO	5935

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EXAMINER	
ZEMAN, ROBERT A	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 03/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/831,627	NALDINI ET AL.	
	Examiner	Art Unit	
	Robert A. Zeman	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment and response filed on 1-5-2006 are acknowledged. Claims 1 and 2 have been amended. Claim 9 has been added. Claims 1-9 are pending. Claim 8 remains withdrawn from consideration as being drawn to a non-elected invention. Claims 1-7 and 9 are currently under examination.

Claim Rejections Withdrawn

The rejection of claim 2 under 35 U.S.C. 112, second paragraph, as being indefinite rendered vague and indefinite by the use of the term "incorporate" is withdrawn in light of the amendment thereto.

Claim Rejections Maintained

35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 1-5 and 7 under 35 U.S.C. 102(b) as being anticipated by Ory et al. (PNAS, 1996, Vol. 93, pages 11400-11406 – IDS-8) is maintained for reasons of record.

The instant claims are drawn to methods of amplifying (propagating) an envelope defective retrovirus by contacting said retrovirus to a cell that comprises a gene that encodes a virus envelope integrated into its genome wherein said envelope gene complements said retrovirus. The instant claims have been amended to recite the limitation that said envelope gene is integrated into the cell's genome. Newly added claims recite the limitations: that the envelope protein is VSVG (claim 4); that the retrovirus comprises an immunodeficiency virus; and that the envelope gene is controlled by an inducible promoter. Moreover, while the instant claims require that the envelope gene be integrated, there is no requirement as to when said integration occurs. Consequently the instant claims only require that the envelope defective virus is amplified (claim 1), that the propagated virus comprises the envelope encoded by the integrated gene within the cell and that said envelope is expressed by said cell.

Applicant argues that Ory is not related to or otherwise suggest screening a vector batch for contaminants. Applicant's arguments have been fully considered and deemed non-persuasive.

The instant claims are drawn to methods of amplifying an envelope-defective retrovirus not methods of screening a vector batch for contaminants. Moreover, Ory et al. disclose the sequential exposure of 293 cells to first a retroviral vector (MuMLV-Env defective) and then subsequently to a plasmid encoding VSV-G envelope protein (see Figure 2). In the context of the claimed methods said plasmid composition constitutes a "vector batch."

As outlined previously, Ory et al. disclose a packaging cell line for the production of high titer retroviruses with VSV G protein (envelope protein) [see abstract]. Ory et al. further disclose the transfecting of cells with a retroviral vector (MuMLV-Env defective) and a plasmid encoding VSV-G envelope protein (see page 11401, 1st column and page 11403). Ory et al. further

disclose the use of an inducible promoter to regulate the expression of the VSVG envelope protein (see page 11402, 1st column). Ory et al. also disclose that said cells expressed VSV-G on its surface (see page 11401, 2nd column and page 11403). The resulting "psuedotypes" (i.e. viruses produced by the transfected cells) contain VSV-G envelope proteins on their surface (see pages 11405-11406). Consequently, Ory et al. anticipates all the limitations of the rejected claims.

The rejection of claims 1-3 and 5-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Gruber et al. (U.S. Patent 5,503,974) is maintained for reasons of record.

Applicant has provided no argument as to why the cited reference does not constitute art. Consequently, the rejection is deemed to be proper and is maintained.

As outlined previously, Gruber et al. disclose a method of amplifying replication deficient retroviruses by bringing said replication deficient retroviruses (which can lack *env)* in contact with cells that have the *env* gene within their genome (see column 6, lines 50-57).

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gruber et al. (U.S. Patent 5,503,974) and Ory et al. (PNAS, 1996, Vol. 93, pages 11400-11406 – IDS-8) for the reasons set forth in the previous Office action in the rejection of claims 1-7.

Applicant argues:

1. The cited references do not involve or suggels use of an indicator cell into which a transgene encoding a virus envelope has been integrated into the genome to detect envelope defective retrovirus and using such an indicator cell line to screen a vector batch for safety and purity.

2. The prior art does not contemplate the development of a screening method having the sensitivity explicitly recited in newly added claim 9.

3. The prior art does not teach or suggest the measurement of defective retrovirus in a vector batch.

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Points 1 and 3, the instant claims are drawn to methods of amplifying an envelope-defective retrovirus not methods of screening a vector batch for contaminants. Moreover, Ory et al. disclose the sequential exposure of 293 cells to first a retroviral vector (MuMLV-Env defective) and then subsequently to a plasmid encoding VSV-G envelope protein (see Figure 2). In the context of the claimed methods said plasmid composition constitutes a

"vector batch." Additionally, Ory discloses the use of NIH 3T3 cells to determine viral titers (see page 11404).

With regard to Point 2, while neither reference explicitly discloses the sensitivity recited in newly added claim 9, it is deemed that since combination of references results in the same method steps as the instant invention, both methods would have the same sensitivities.

The instant claims are drawn to methods of amplifying (propagating) an envelope defective retrovirus by contacting said retrovirus to a cell that comprises a gene that encodes a virus envelope integrated into its genome wherein said envelope gene complements said retrovirus. The instant claims have been amended to recite the limitation that said envelope gene is integrated into the cell's genome. Newly added claims recite the limitations: that the envelope protein is VSVG (claim 4); that the retrovirus comprises an immunodeficiency virus; and that the envelope gene is controlled by an inducible promoter. Moreover, while the instant claims require that the envelope gene be integrated, there is no requirement as to when said integration occurs. Consequently the instant claims only require that the envelope defective virus is amplified (claim 1), that the propagated virus comprises the envelope encoded by the integrated gene within the cell and that said envelope is expressed by said cell.

As outlined previously, Gruber et al. disclose a method of amplifying replication deficient retroviruses by bringing said replication deficient retroviruses (which can lack *env)* in contact with cells that have the *env* gene within their genome (see column 6, lines 50-57).

Gruber et al. differs from the instant invention in that they don't disclose the use of GVSG as the viral envelope gene (*env).*

Ory et al. disclose a packaging cell line for the production of high titer retroviruses with VSV G protein (envelope protein) [see abstract]. Ory et al. further disclose the transfecting of cells with a retroviral vector (MuMLV-Env defective) and a plasmid encoding VSV-G envelope protein (see page 11401, 1st column and page 11403). Ory et al. further disclose the use of an inducible promoter to regulate the expression of the VSVG envelope protein (see page 11402, 1st column). Ory et al. also disclose that said cells expressed VSV-G on its surface (see page 11401, 2nd column and page 11403). The resulting "psuedotypes" (i.e. viruses produced by the transfected cells) contain VSV-G envelope proteins on their surface (see pages 11405-11406).

It would have been obvious for one of skill in the art to use the VSV G envelope protein/gene disclosed by Ory et al. in the method disclosed by Gruber et al. in order to take advantage of broader tropism associated with VSVG.

New Claim Rejections

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 and 9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicant has amended the claim to recite "a vector batch to be screened for the presence of exogenous envelope-defective retrovirus". This phrase does not appear in the specification, or original claims as filed. Applicant points to a portion of the specification as the specific basis for this limitation however, said phrase is not used in the context of the claimed method and hence cannot serve as support for said phrase. Therefore this limitation is new matter.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

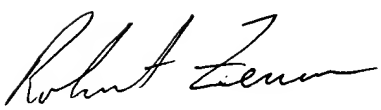
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



ROBERT ZEMAN
PATENT EXAMINER

March 10, 2006